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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,504	11/03/2006	Jonas Lundahl	05432/1201132-US1	9987
7278	7590	06/16/2009	EXAMINER	
DARBY & DARBY P.C. P.O. BOX 770 Church Street Station New York, NY 10008-0770			PHILLIPS JR, WELDON P	
			ART UNIT	PAPER NUMBER
			1614	
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			06/16/2009	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/599,504	<b>Applicant(s)</b> LUNDAHL ET AL.	
	<b>Examiner</b> WELDON P. PHILLIPS JR.	<b>Art Unit</b> 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 27 April 2009.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 23 and 25-51 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 23 and 25-51 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Response to Arguments***

Applicants' arguments, filed April 27, 2009, have been fully considered but they are not persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set being applied to the instant application.

#### ***Claim Objections***

The objection to claim 24 as being a duplicate of claim 23 is now moot in light of applicants' cancellation of claim 24.

#### ***Claim Rejections – 35 U.S.C. 112 2nd Paragraph***

Applicants' arguments with respect to the rejection of claims under 35 U.S.C. 112 2nd paragraph have been fully considered and found persuasive. As such, the rejection of claims 40-42, as previously drafted, is hereby withdrawn.

#### ***Claim Rejections – 35 U.S.C. 103***

Applicants' arguments with respect to the rejection of claims 23-28 and 39-42 under 35 U.S.C. 103 have been fully considered but they are not persuasive:

**Claims 23, 25-28 and 39-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Radulovacki [WO 00/51590 (2000), cited on IDS dated**

Art Unit: 1614

**November 28, 2006], in view of Lancel [USPN 5,929,065 (1999), cited on PTO-892 dated January 9, 2009].**

The rejection is maintained for the reasons of record. The rejection of claim 24 is now moot in light of applicants' cancellation of claim 24. The rejection of claims 40-42 extends to the amended claims for the reasons already of record, as each of the claim limitations were explicitly interpreted in light of the explicit definitions present in the specification, said explicit definitions now being present in the amended claims.

Applicant first argues that, in spite Radulovacki's teachings with respect to preventing or ameliorating sleep-related breathing disorders including sleep apnea with GABA agonists including gaboxadol, Radulovacki recites zolpidem as a suitable compound for use in its methods of treating sleep apnea while there is clinical data showing that not all GABA agonists, e.g., zolpidem, are suitable for treating sleep apnea. Specifically, applicants point to an abstract of a study published by Cirignotta in 1988 (Exhibit B) wherein a single dose of 20 mg of zolpidem did not overcome alleged contraindications for using hypnotics in sleep apnea syndrome and that the 2008 Ambien® label (Exhibit A) contains the statement that Ambien® "should be used with caution in patients suffering with sleep apnea syndrome." Applicant further argues that sleep disorders, e.g., insomnia, are different from breathing disorders, e.g., sleep apnea, such that one of ordinary skill in the art would not be able to reasonably predict whether any one particular GABA receptor agonist, e.g., gaboxadol, would be successful in treating both disorders and that based on the teachings of Cirignotta (Exhibit B) and the Ambien® label (Exhibit A), one of ordinary skill in the art would have

Art Unit: 1614

been discouraged from using any hypnotic compound, e.g., gaboxadol, in an effort to treat sleep apnea with any expectation of success. Finally, applicant argues that since Lancel discloses the use of gaboxadol as a hypnotic, makes no mention of respiratory disorders, any impact on sleep apnea or any other sleep disorder that is specifically breathing-related, Lancel fails to cure the deficiencies of Radulovacki.

Ascertaining the differences between the prior art and the claims at issue requires interpreting the claim language, and considering both the invention and the prior art references as a whole. A prior art reference that “teaches away” from the claimed invention is a significant factor to be considered in determining obviousness; however, “the nature of the teaching is highly relevant and must be weighed in substance. The decision on patentability must be made based upon consideration of all the evidence, including the evidence submitted by the examiner and the evidence submitted by the applicant. Obviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness. In re Rinehart, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976).

With respect to the applicants’ first argument, the examiner notes that Exhibit A and B relate to a GABA agonist, e.g., zolpidem, which is not the subject of the instant application, claims or prior office action. Nevertheless, since zolpidem is taught and claimed by Radulovacki with 12 other exemplary GABA agonists, including gaboxadol, as being useful in the treatment of sleep-related breathing disorders such as sleep apnea (p. 17, lines 3-5 and 12-13; p. 18, lines 5-9; claims 15-18), the expectation of

Art Unit: 1614

success, or lack thereof, with other GABA agonists taught by Radulovacki, e.g. zolpidem, is relevant to the question of obviousness of the instant claims. The examiner has considered Exhibit A and Exhibit B, particularly the conclusion of the study in Exhibit B that a 20 mg dose of zolpidem did not overcome the alleged contraindications for using hypnotics in sleep apnea syndrome and the statements on Exhibit A that a dose of 10 mg zolpidem reduced Total Arousal Index, lowest oxygen saturation and increased the number of times oxygen saturation dropped below 80% and 90% in patients with mild-to-moderate sleep apnea and that Ambien® “should be used with caution in patients with sleep apnea syndrome,” present in Section 5 entitled Warnings and Precautions / 5.6 Special Populations (p. 4-5), not Section 4 which is entitled Contraindications (p. 2). Few, if any, pharmaceutical agents are without unwanted side effects. Many, if not most, have narrow therapeutic windows, wherein the dose administered provides efficacy that outweighs the adverse effects elicited by the agent. Zolpidem is - unremarkably - no different from other agents in this regard. The examiner notes that gaboxadol has had its own difficulties in insomnia efficacy trials with notable safety concerns.

With respect to the applicants' second argument, the examiner is well aware that sleep disorders are different from breathing disorders and sleep-related breathing disorders. Radulovacki teaches and claims 13 specie of specifically identified GABA agonists, including gaboxadol, which are useful in the treatment of the sleep-related breathing disorder sleep apnea (p. 17, lines 3-5 and 12-13; p. 18, lines 5-9; claims 15-18). Whether one of ordinary skill in the art would be reasonably able to predict, based

Art Unit: 1614

on the teachings of Radulovacki in view of Lancel, which GABA receptor agonists would be successful in treating sleep disorders is irrelevant to whether one would be able to predict which GABA agonists would be reasonably expected to successfully treat the sleep-related breathing disorder sleep apnea. The examiner has balanced the teachings of Exhibits A and B in light of the teachings of Radulovacki in view of Lancel. Although Exhibit A suggests caution in administering zolpidem to sleep apnea patients and the conclusion of the study summarized by Exhibit B that a 20 mg dose of zolpidem did not overcome the alleged contraindications for using hypnotics in sleep apnea syndrome, these statements do little to overcome the specificity with which Radulovacki teaches that gaboxadol is useful in treating sleep apnea.

With respect to the applicants' final argument, applicant is reminded that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In *re* Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In *re* Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Each of the claims were rejected based on the combination of Radulovacki and Lancel, wherein Lancel was combined with Radulovacki to teach (1) that daily administration of gaboxadol was known, (2) that increased slow-wave or non-REM sleep after treatment with gaboxadol was known, (3) that gaboxadol's suitability for treatment of the elderly was known, and (4) that daily administration of gaboxadol without a suggestion of treatment duration was known, each of which addressed administration limitations which were either not explicitly taught by Radulovacki or related to the properties of gaboxadol.

As such, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Radulovacki and Lancel to create the claimed invention of claims 23, 25-28 and 39-42 with a reasonable expectation of success.

Applicants' arguments with respect to the rejection of claim 29 under 35 U.S.C. 103 have been fully considered but they are not persuasive:

**Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Radulovacki in view of Lancel, as applied to claims 23, 25-28 and 39-42 above, and further in view of Vandeputte [Sleep disorders and depressive feelings: a global survey with the Beck depression scale, Sleep Medicine 4, 343-345 (2003), cited on PTO-892 dated January 9, 2009] and Sanchez [The effects of continuous positive air pressure treatment on anxiety and depression levels in apnea patients, Psychiatry and Clin. Neurosci. 55, 641-646 (2001), cited on PTO-892 dated January 9, 2009].**

The rejection is maintained for the reasons of record.

Applicant argues that since neither Vandeputte nor Sanchez disclose the use of gaboxadol to treat sleep apnea, Vandeputte and Sanchez, like Lancel, fail to cure the deficiencies of Radulovacki.

Applicant is reminded that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc., 800 F.2d

Art Unit: 1614

1091, 231 USPQ 375 (Fed. Cir. 1986). Claim 29 was rejected based on the combination of Radulovacki, Lancel, Vandeputte and Sanchez, wherein Lancel, Vandeputte and Sanchez were combined with Radulovacki for the reasons of record.

As such, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Radulovacki, Lancel, Vandeputte and Sanchez to create the claimed invention of claim 29 with a reasonable expectation of success.

Applicants' arguments with respect to the rejection of claims 30-32 and 43 under 35 U.S.C. 103 have been fully considered but they are not persuasive:

**Claims 30-32 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Radulovacki in view of Lancel, as applied to claims 23, 25-28 and 39-42 above, and further in view of the Krogsgaard-Larsen patent [EP 0000338 (1981), cited on IDS dated November 28, 2006] and Ebert [WO 02/40009 (2002), cited on PTO-892 dated January 9, 2009].**

The rejection is maintained for the reasons of record.

Applicant argues that since neither the Krogsgaard-Larsen patent nor Ebert disclose the use of gaboxadol to treat sleep apnea, the Krogsgaard-Larsen patent and Ebert, like Lancel, fail to cure the deficiencies of Radulovacki.

Applicant is reminded that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc., 800 F.2d

Art Unit: 1614

1091, 231 USPQ 375 (Fed. Cir. 1986). Claims 30-32 and 43 were rejected based on the combination of Radulovacki, Lancel, the Krogsgaard-Larsen patent and Ebert, wherein Lancel, the Krogsgaard-Larsen patent and Ebert were combined with Radulovacki for the reasons of record.

As such, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Radulovacki, Lancel, the Krogsgaard-Larsen patent and Ebert to create the claimed invention of claims 30-32 and 43 with a reasonable expectation of success.

Applicants' arguments with respect to the rejection of claims 33-38 and 44-48 under 35 U.S.C. 103 have been fully considered but they are not persuasive:

**Claims 33-38 and 44-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Radulovacki in view of Lancel, as applied to claims 23, 25-28 and 39-42 above, and further in view of the Krogsgaard-Larsen patent.**

The rejection is maintained for the reasons of record.

Applicant argues that since the Krogsgaard-Larsen patent does not disclose the use of gaboxadol to treat sleep apnea, the Krogsgaard-Larsen patent, like Lancel, fail to cure the deficiencies of Radulovacki.

Applicant is reminded that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Claims 33-38 and 44-48 were rejected based on

Art Unit: 1614

the combination of Radulovacki, Lancel and the Krogsgaard-Larsen patent, wherein Lancel and the Krogsgaard-Larsen was combined with Radulovacki for the reasons of record.

As such, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Radulovacki, Lancel and the Krogsgaard-Larsen patent to create the claimed invention of claims 33-38 and 44-48 with a reasonable expectation of success.

Applicants' arguments with respect to the rejection of claims 49-51 under 35 U.S.C. 103 have been fully considered but they are not persuasive:

**Claims 49-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Radulovacki in view of Lancel and the Krogsgaard-Larsen patent, as applied to claims 33-38 and 44-48 above, and further in view of the Krogsgaard-Larsen reference [THIP, a specific and clinically active GABA agonist, Neuropharm. 23, 837-838 (1984), cited on IDS dated November 28, 2006] and Elema [WO 01/22941 (2001), cited on PTO-892 dated January 9, 2009]**

The rejection is maintained for the reasons of record.

Applicant argues that since neither the Krogsgaard-Larsen reference nor Elema disclose the use of gaboxadol to treat sleep apnea, the Krogsgaard-Larsen reference and Elema, like Lancel and the Krogsgaard-Larsen patent, fail to cure the deficiencies of Radulovacki.

Applicant is reminded that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Claims 49-51 were rejected based on the combination of Radulovacki, Lancel, the Krogsgaard-Larsen patent, the Krogsgaard-Larsen reference and Elema, wherein Lancel, the Krogsgaard-Larsen patent, the Krogsgaard-Larsen reference and Elema were combined with Radulovacki for the reasons of record.

As such, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Radulovacki, Lancel, the Krogsgaard-Larsen patent, the Krogsgaard-Larsen reference and Elema to create the claimed invention of claims 49-51 with a reasonable expectation of success.

### ***Claim Disposition***

Claims 23 and 25-51, as amended, are rejected at this time. No claims are allowed.

### ***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

Art Unit: 1614

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to WELDON P. PHILLIPS JR. whose telephone number is (571)-270-7673. The examiner can normally be reached Monday through Thursday between 8:30 AM and 7:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached at 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Application/Control Number: 10/599,504  
Art Unit: 1614

Page 13

/WP/  
Examiner, Art Unit 1614

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